REMARKS

Claims 1, 2 and 25 were pending in the present case. Claims 1 and 25 have been amended[1], Claim 2 has been cancelled, and Claims 26-43[2] have been added. As such, Claims 1, 25, and 26-45 are currently pending in the present case. The pending claims are attached at Appendix 2 for the Examiner's convenience.

In the Final Office Action dated January 18, 2002 ("Final Office Action"), the Examiner rejected the claims, while referring to the Office Action dated September 13, 2001 ("Previous Office Action") to provide the reasons for these rejections. Therefore, the rejections in the Previous Office Action are addressed below. For clarity, the rejections at issue are set forth by number in the order they are herein addressed:

(1) Claims 1 and 25 were rejected under 35 U.S.C. 102(e), as allegedly being anticipated by Muir *et al.*; and

(2) Claims 1, 2 and 25 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Muir *et al.* in view of Gaur *et al.*, Goodwin *et al.*, and Oprandy.

Applicants believe the amendments made above and the following remarks traverse the Examiner's rejections of the Claims. These remarks are presented in the same order as the above rejections.

I. The Claims are Not Anticipated

Claims 1 and 25 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Pat. 5,891,435 to Muir *et al.* Applicants respectfully disagree with this rejection.

The Examiner states that Muir *et al.* "teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used ... ." (Previous Office Action, pg 2).

---

[1] Support for these amendments may be found in the Specification, for example, in Example 2 at pages 16 and 17 (see, Table 4, where the inflammatory cytokine IFNγ and non-inflammatory cytokine IL-5 are assayed to determine which type of cytokine is primarily expressed by the T cells).

[2] Support for these claims may be found in the Specification at, for example, pg 7, lines 13-23, pages 8-9, and Example 2, pgs 16-17.

Applicants note, however, that Muir *et al.* does not provide any examples employing MBP with IFA (e.g. in order to treat MS type symptoms in an animal model). As such, Applicants submit that the Examiner's reliance on Muir *et al.* is not proper, but instead is a classic "obvious to try" or "obvious to experiment" type rejection. The Federal Circuit has consistently held that "obvious to try" does not properly form the basis of a rejection, stating:

> "[a]n "obvious-to-try situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued" (*Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, Fed. Cir. 1990).

Even assuming *arguendo* that Muir *et al.* provided the required teaching, this reference still does not indicate that the claimed result would be obtained (*e.g.*. Muir et al. fails to provide any working examples relating to MBP in IFA to treat MS). For example, Muir *et al.* not only mentions treating MS with an antigen and IFA, but also mentions fifteen other diseases that may allegedly be treated or prevented by an antigen and IFA. These other diseases, besides MS, that allegedly may be treated include:

1. autoimmune uveitis,
2. rheumatoid arthritis,
3. Addison's disease,
4. thyroiditis,
5. Graves' disease,
6. atrophic gastritis,
7. myasthenia gravis,
8. idiopathic thrombocytopenic purpura,
9. hemolytic anemia,
10. systemic lupus erythematosus,
11. primary biliary cirrhosis,
12. Wegener's granulomatosis,
13. polyarteritis nodosa,
14. inflammatory bowel disease, and
15. type 1 diabetes

However, despite this shopping list of diseases that one might treat or prevent, Muir *et al.* fails to provides ANY evidence that 14 of these 15 diseases (i.e. all of the above except type 1 diabetes) could successfully be treated with an antigen and IFA. In other words, Muir *et al.* simply indicates that ONE MIGHT TRY treating one of these 14 untested diseases, but fails to provide ANY evidence that one would be successful in treating any of these diseases except for type 1 diabetes.

In light of the above, Applicants submit that the Examiner's rejection should be withdrawn. Nonetheless, for business reasons, and in order to further the prosecution of the present Application, yet without acquiescing to any of the Examiner's arguments, and while explicitly reserving the right to prosecute the original claims (or similar claims) in the future, Applicants have amended Claims 1 and 25. In particular, Claims 1 and 25 now recite two additional steps (step "c" of obtaining T cells from the immunized human, and step "d" determining if the T cells from the patient are primarily Th2 cells secreting anti-inflammatory cytokines or Th 1 cells secreting inflammatory cytokines, with the presence of Th2 indicating that the immunization is protective against MS). Muir *et al.* does not teach obtaining a T cell sample from an immunized human, let alone suggesting why one would want to determine what type T cell response was being generated. As such, Muir *et al.* fails to anticipate these claims, and this rejection should be removed.

II. The Claims are Not Obvious

The Examiner rejected Claims 1, 2, and 25 under 103(a) as being unpatentable over Muir *et al.*, in view of Gaur *et al.*, Goodwin *et al.* (U.S. Pat., 5,569,585) and Oprandy (U.S. Pat. 5,200,312) (Previous Office Action, pg 3). Applicants disagree with this rejection. However, Applicants submit that this rejection is moot as Claim 2 has been cancelled and Claims 1 and 25 have been amended.

Applicants submit that the Examiner could not establish a *prima facie* case of obviousness for amended Claims 1 and 25, or for new claims 26-45. For example, all of the pending claims recite methods for monitoring immunity generated by immunization with MBP and IFA. Moreover, Claims 1 and 25 recite determining if the T cells from the patient are primarily Th2 cells secreting anti-inflammatory cytokines or Th 1 cells secreting inflammatory cytokines, with the presence of Th2 indicating that the immunization is

protective against MS. None of the references provide a motivation to test a patient sample to determine what cytokines are being expressed, let alone determining if anti-inflammatory or inflammatory cytokines are being expressed (i.e. none of the references suggest reasons why such a test would be conducted). The Examiner might attempt to argue that such a test COULD be performed. However, this is not the standard. Instead, in order to establish a motivation to combine, the Examiner must point to a suggestion in the references establishing why one WOULD combine the references in such a fashion. Applicants submit that no such motivation exists as required by MPEP 2143.01. As such, the Claims should be allowed since no *prima facie* case of obviousness could be established.

Applicants also note that the combined references would not teach that the presence of Th2 cells expressing anti-inflammatory cytokines in a sample as indicating that immunization with MBP and IFA is protective against MS. As such, the combined art would not teach all of the claim limitations as required by MPEP 2143.03. Therefore, the Claims should be allowed since no *prima facie* case of obviousness could be established.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants' claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (618) 218-6900.

Dated: April 30, 2002

Jason R. Bond
Registration No. 45,439
MEDLEN & CARROLL, LLP
110 Howard Street, Suite 350
San Francisco, California 94105
(608) 218-6900

Appendix 1 - Version With Markings to Show Changes Made

IN THE SPECIFICATION:

Title beginning at line 1, page 1, has been amended as follows:

[METHODS OF INDUCING IMMUNITY] METHODS OF MONITORING IMMUNIZATION

IN THE CLAIMS:

1. (amended) A method of monitoring immunization [immunizing a human], comprising:

a) providing: i) a human, and ii) an immunizing preparation comprising myelin basic protein and Incomplete Freund's Adjuvant; [and]

b) immunizing said human with said immunizing preparation [under conditions such that said immunization is protective against multiple sclerosis.];

c) obtaining a primary cell population from said human comprising T cells capable of secreting cytokines; and

d) determining if said T cells are primarily Th2 cells secreting an anti-inflammatory cytokine or primarily Th1 cells secreting an inflammatory cytokine, wherein said Th2 cells secreting an anti-inflammatory cytokine indicates that said immunizing is protective against multiple sclerosis.

25. (amended) A method of monitoring immunization [immunizing a human], comprising:

a) providing: i) a human with symptoms of multiple sclerosis, and ii) an immunizing preparation comprising myelin basic protein and Incomplete Freund's Adjuvant; [and]

b) immunizing said human with said immunizing preparation [under conditions such that said symptoms are reduced.];

c) obtaining a primary cell population from said human comprising T cells capable of secreting cytokines; and

d) determining if said T cells are primarily Th2 cells secreting an anti-inflammatory cytokine or primarily Th1 cells secreting an inflammatory cytokine, wherein said Th2 cells secreting an anti-inflammatory cytokine indicates that said immunizing is effective for treating symptoms of multiple sclerosis.

Appendix 2 - Pending Claims

1. A method of monitoring immunization, comprising:

a) providing: i) a human, and ii) an immunizing preparation comprising myelin basic protein and Incomplete Freund's Adjuvant;

b) immunizing said human with said immunizing preparation;

c) obtaining a primary cell population from said human comprising T cells capable of secreting cytokines; and

d) determining if said T cells are primarily Th2 cells secreting an anti-inflammatory cytokine or primarily Th1 cells secreting an inflammatory cytokine, wherein said Th2 cells secreting an anti-inflammatory cytokine indicates that said immunizing is protective against multiple sclerosis.

25. A method of monitoring immunization, comprising:

a) providing: i) a human with symptoms of multiple sclerosis, and ii) an immunizing preparation comprising myelin basic protein and Incomplete Freund's Adjuvant;

b) immunizing said human with said immunizing preparation;

c) obtaining a primary cell population from said human comprising T cells capable of secreting cytokines; and

d) determining if said T cells are primarily Th2 cells secreting an anti-inflammatory cytokine or primarily Th1 cells secreting an inflammatory cytokine, wherein said Th2 cells secreting an anti-inflammatory cytokine indicates that said immunizing is effective for treating symptoms of multiple sclerosis.

26. A method of monitoring immunization, comprising:

a) providing: i) a human, and ii) an immunizing preparation comprising myelin basic protein and Incomplete Freund's Adjuvant;

b) immunizing said human with said immunizing preparation;

c) obtaining a primary cell population from said human comprising T cells capable of secreting cytokines;

d) adding said primary cell population to a microwell comprising a hydrophobic membrane having a first cytokine binding ligand, under conditions such that said T cell secretes a cytokine that binds to said first cytokine binding ligand;

e) adding a second cytokine binding ligand to said microwell under conditions such that said cytokine binding ligand binds to said cytokine; and

f) detecting said secreted cytokine, thereby monitoring said immunizing.

27. The method of Claim 26, wherein said detected cytokine is IL-5.

28. The method of Claim 26, wherein said detected cytokine is IL-4.

29. The method of Claim 26, wherein said detected cytokine is IL-10.

30. The method of Claim 26, wherein said detected cytokine is IFNγ.

31. The method of Claim 26, wherein said detected cytokine is IL-2.

32. The method of Claim 26, wherein said hydrophobic membrane comprises polyvinylidene difluoride.

33. The method of Claim 26, wherein said microwell comprises an enclosed bottom.

34. The method of Claim 1, wherein said determining comprises detecting said secreted cytokine.

35. The method of Claim 1, wherein said secreted cytokine is IL-5.

36. The method of Claim 1, wherein said secreted cytokine is IL-4.

37. The method of Claim 1, wherein said secreted cytokine is IL-10.

38. The method of Claim 1, wherein said secreted cytokine is IFNγ.

39. The method of Claim 1, wherein said secreted cytokine is IL-2.

40. The method of Claim 25, wherein said determining comprises detecting said secreted cytokine.

41. The method of Claim 25, wherein said secreted cytokine is IL-5.

42. The method of Claim 25, wherein said secreted cytokine is IL-4.

43. The method of Claim 25, wherein said secreted cytokine is IL-10.

44. The method of Claim 25, wherein said secreted cytokine is IFNγ.

45. The method of Claim 25, wherein said secreted cytokine is IL-2.